

## Comparison of Pulsed CO<sub>2</sub> Laser Ablation at 10.6 $\mu\text{m}$ and 9.5 $\mu\text{m}$

Barry P. Payne, SM,<sup>1,2\*</sup> Norman S. Nishioka, MD,<sup>1</sup> Bora B. Mikic, ScD,<sup>2</sup> and Vasan Venugopalan, ScD<sup>1,2,3</sup>

<sup>1</sup>Wellman Laboratories of Photomedicine, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts 02114

<sup>2</sup>Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

<sup>3</sup>Beckman Laser Institute, University of California, Irvine, Irvine, California 92612

**Background and Objective:** The pulsed CO<sub>2</sub> laser has received attention because of its successful application to dermatologic surgery and burn debridement surgery. Despite impressive results, tissue removal using pulsed CO<sub>2</sub> laser irradiation has not been optimized. We examined the ablation processes by performing mass removal and thermal injury experiments at wavelengths where tissue water is the primary absorber (10.6  $\mu\text{m}$ ), and where water and collagen have comparable absorption (9.5  $\mu\text{m}$ ).

**Study Design/Materials and Methods:** Samples of porcine reticular dermis were irradiated with 180-ns laser pulses at either wavelength. Tissue removal was measured using a digital balance. Thermal injury was assessed using a microscope with a calibrated reticle after hematoxylin and eosin staining.

**Results:** Tissue removal using 10.6- $\mu\text{m}$  radiation resulted in a heat of ablation of 3,740 J/g, an ablation threshold of 1.15 J/cm<sup>2</sup>, and a zone of thermal injury of 53  $\mu\text{m}$ . By contrast, tissue removal using 9.5- $\mu\text{m}$  radiation resulted in a heat of ablation of 3,330 J/g, an ablation threshold of 1.47 J/cm<sup>2</sup>, and a zone of thermal injury of 34  $\mu\text{m}$ . The differences in ablation threshold and thermal injury were statistically significant.

**Conclusion:** Pulsed CO<sub>2</sub> laser irradiation at 9.5  $\mu\text{m}$  removes tissue more efficiently and with a smaller zone of thermal injury than at 10.6  $\mu\text{m}$ . *Lasers Surg. Med.* 23:1–6, 1998.

© 1998 Wiley-Liss, Inc.

**Key words:** heat of ablation; laser ablation efficiency; explosive vaporization; thermal injury

### INTRODUCTION

The carbon dioxide (CO<sub>2</sub>) laser has been widely used in medical applications because of its ability to coagulate, incise, and excise biological tissue. Recently, the pulsed CO<sub>2</sub> laser has received attention because of its successful application to skin surgery and burn debridement. Although continuous wave (cw) CO<sub>2</sub> lasers were used in the 1980s and early 1990s, the high degree of thermal injury produced during ablation (200–1,000  $\mu\text{m}$ ) caused unpredictable results with

an increased risk of scarring. High-energy pulsed CO<sub>2</sub> lasers or rapidly scanned cw lasers limit thermal diffusion during ablation and therefore decrease thermal injury to approximately 70–160

Contract grant sponsor: Whitaker Foundation (Biomedical Engineering Research Grant; Contract grant sponsor: National Center for Research Resources (NIH); Contract grant number: RR-01192.

\*Correspondence to: Barry Payne, Massachusetts General Hospital, M/S BH 703, 50 Blossom St., Boston, MA 02114. E-mail: bugzy@mit.edu

Accepted 17 April 1998

$\mu\text{m}$  [1]. Despite widespread clinical use, tissue removal with pulsed  $\text{CO}_2$  laser irradiation continues to generate thermal injury in excess of that which is necessary to produce hemostasis, often causing temporary and sometimes permanent side effects such as hyperpigmentation, hypopigmentation, edema, and erythema (eg. [2,3]). While pre- and post-treatment therapies can reduce healing time [4], optimization of the laser system to control depth of thermal injury for surgical procedures would be beneficial.

Unlike infrared lasers, ultraviolet lasers tend to remove tissue cleanly, efficiently, and with minimal thermal injury [5,6]. Recent work has suggested that tissue chromophore may be responsible for the disparate effects produced by different laser wavelengths [7–9]. It has been observed that when collagen is directly targeted by choosing an appropriate wavelength such as 193 nm and 248 nm, material removal is consistent with a process of rapid surface vaporization [7]. However, when tissue water is targeted by using infrared wavelengths such as 2.79  $\mu\text{m}$  and 10.6  $\mu\text{m}$ , a delayed and more explosive ablation process is observed [8]. Because ultraviolet lasers produce high-energy photons, some investigators have postulated optical and photochemical phenomena to explain ablation processes occurring during ultraviolet laser ablation [10–15]. However, Edwards and co-workers have provided evidence that low photon energies can also produce clean and efficient ablation events by targeting the amide II band of collagen at 6.45  $\mu\text{m}$  [9]. Although 6.45  $\mu\text{m}$  lasers are not broadly available, other laser lines could be used to target collagen.

The  $\text{CO}_2$  laser is capable of producing high-energy pulses at wavelengths in the 9–11  $\mu\text{m}$  region. The absorption spectra of dry collagen [16] and water [17] within the  $\text{CO}_2$  laser wavelength range are shown in Figure 1. At the laser wavelength used in most  $\text{CO}_2$  laser applications (10.6  $\mu\text{m}$ ), the dominant chromophore is water, whereas at 9.5  $\mu\text{m}$ , the absorption of collagen and tissue water are comparable. We therefore hypothesized that irradiation at 9.5  $\mu\text{m}$  would affect a more efficient ablation process with less thermal injury. The purpose of this study was to test this hypothesis by comparing clinically relevant parameters such as ablation efficiency, ablation threshold, and depth of thermal injury for pulsed  $\text{CO}_2$  laser irradiation at wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ .

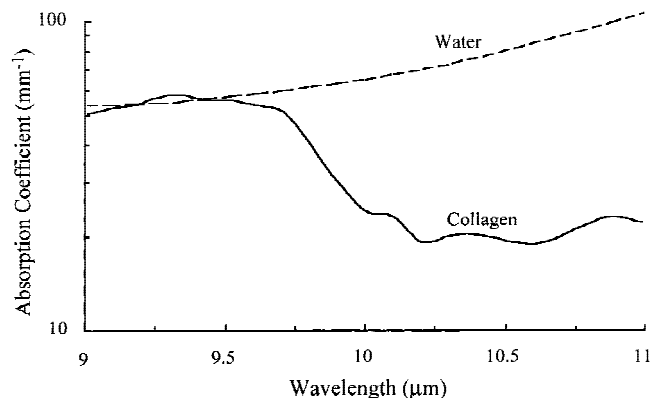


Fig. 1. Absorption spectra for dry collagen and water in the far IR region.

## MATERIALS AND METHODS

### Laser

A nitrogen-starved tunable transversely excited atmospheric (TEA)  $\text{CO}_2$  laser (840, Lumonics, Kanata, Ontario) was used for all experiments. The laser wavelength was selected by tuning a diffraction grating at the rear of the laser cavity. The diffraction grating was calibrated using a  $\text{CO}_2$  spectrum analyzer (Laser Craft, Santa Rosa, CA). The temporal width of the laser pulse consisted of a single 180-ns pulse (full-width half-maximum) with no observable tail as measured by a pyroelectric detector with a response time of 500 ps (P5-02, Molelectron Detector, Portland, OR). The laser output was horizontally polarized with a pulse to pulse energy variation of less than 4%. A uniform portion of the laser beam was selected with a 15-mm aperture and focused onto the target by a 203-mm focal length ZnSe lens. Attenuators were used to vary the incident energy that reached the tissue target, and a helium-neon laser coupled with a beamsplitter was used to identify the ablation plane [18]. The spatial profile of the laser beam was measured by stepping through the ablation plane with a 300- $\mu\text{m}$ -diameter aperture and measuring the transmitted energy using a pyroelectric detector (J3-09, Molelectron Detector, Portland, OR). The  $1/e^2$  diameters were calculated using a gaussian least-mean-squares fit and were 2.68 mm and 2.44 mm for wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ , respectively. The difference in spot sizes were due to slight differences in laser mode and the refractive index of ZnSe at 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$  wavelengths.

### Tissue Removal Experiments

Sections of porcine reticular dermis approximately 4-mm thick were excised immediately postmortem and irradiated within 12 hours. Prior to irradiation, 6-mm biopsy punch samples were obtained and placed in a plastic holder on the pan of a digital balance (AE163, Mettler Instrument Corp., Hightstown, NJ) so that all ablated material would land off the pan [18]. Twelve pulses at 1 Hz were delivered in sequence to each tissue sample. The number of pulses was held constant at 12 to ensure sufficient mass removal but minimize tissue dehydration during the experiment. Mass loss data were acquired using a personal computer at 2.4 Hz using data acquisition software (LabView, National Instruments, Austin, TX).

### Thermal Injury Experiments

The experimental setup was identical with the tissue removal setup, except that a digital balance and computer were not used. The energy delivered to the tissue target was chosen based on two criteria. First, the pulse energy was normalized with respect to ablation threshold as determined from the tissue removal experiments. Second, the pulse energy was as high as possible without causing plasma formation. The radiant exposures that satisfied these conditions were 3.5 J/cm<sup>2</sup> and 4.5 J/cm<sup>2</sup> for wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ , respectively. Fifteen tissue samples were irradiated at each wavelength, and the number of pulses delivered to each sample was held constant at 12. After laser irradiation, the tissue samples were fixed in formalin, set in paraffin, cut into 15- $\mu\text{m}$ -thick sections, and stained with hematoxylin and eosin. Thermal injury was assessed by a pathologist who was blinded to the laser parameters used. Thermal injury was measured at the base of each crater using a calibrated reticle to eliminate edge effects.

## RESULTS

### Tissue Removal Experiments

Figure 2 shows a typical plot of the mass lost as recorded by the digital balance versus time. Before the tissue is irradiated, mass removal due to water evaporation from the tissue surface is seen. Once irradiation commences, an increased rate of mass removal is observed due to ablation. After irradiation is complete, mass removal continues due to evaporation. A linear regression

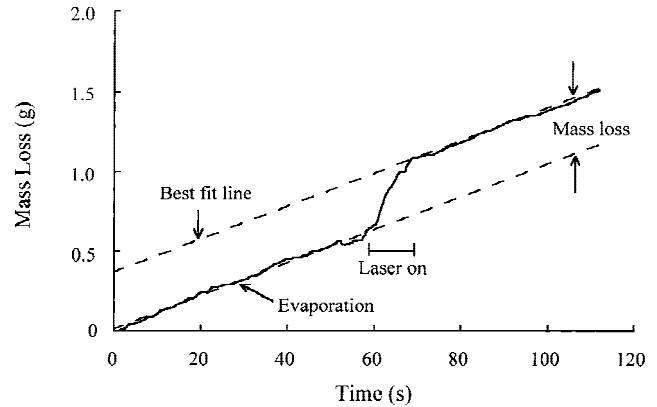


Fig. 2. Typical mass loss versus time curve for TEA CO<sub>2</sub> irradiation. Twelve pulses at 1 Hz were delivered to the porcine dermis target. Mass removal before and after laser irradiation is due to evaporation.

analysis was performed on the mass loss data before and after ablation. The y-intercepts were calculated using the average of the slopes to yield a total corrected mass loss which is shown versus radiant exposure in Figure 3. Optical breakdown or plasma formation (visually observed as a bright white flash) was seen at radiant exposures above 3.7 J/cm<sup>2</sup> and 4.8 J/cm<sup>2</sup> for wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ , respectively. A linear regression analysis was performed on the data for radiant exposures where optical breakdown was not observed. The resulting least-squares fit is shown in Figure 4. The slope of the line represents mass removed per unit energy delivered, and we define this as ablation efficiency ( $\mu\text{g}/\text{J}$ ). The heat of ablation is the reciprocal of the ablation efficiency and is the energy required to remove a unit mass of tissue. The x-intercept is the minimum energy required to achieve material removal and is known as the ablation threshold (J/cm<sup>2</sup>). A summary of the regression and ablation parameters is shown in Table 1. Although the difference in ablation efficiency at the two wavelengths was not quite statistically significant, repeated experiments exhibited the same bias. The difference in ablation threshold was statistically significant ( $P = .005$ ).

### Thermal Injury Experiments

Typical histological sections are shown in Figure 5. The difference between normal and thermally altered tissue is evident by the change in tissue staining. At 9.5  $\mu\text{m}$ , the ablation results in a smoother crater with a more superficial zone of thermal injury when compared to 10.6  $\mu\text{m}$ . The

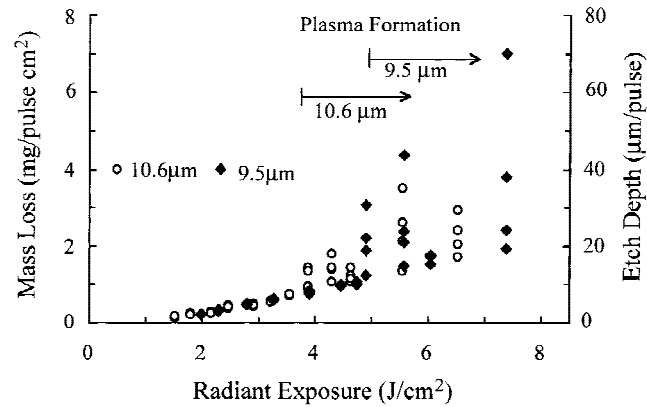


Fig. 3. Mass of porcine dermis removed per pulse per unit area versus laser radiant exposure by a TEA CO<sub>2</sub> laser at wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ . The spread of the data at higher radiant exposures is due to plasma formation.

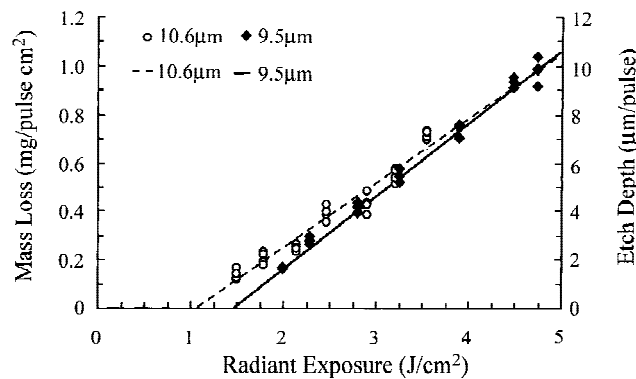


Fig. 4. Mass of porcine dermis removed per pulse per unit area versus laser radiant exposure by a TEA CO<sub>2</sub> laser at wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ . Data are fit to a linear regression before optical breakdown was observed.

**TABLE 1. Linear Regression and Ablation Parameters**

| Wavelength                  | 10.6 $\mu\text{m}$                                 | 9.5 $\mu\text{m}$                                  |
|-----------------------------|--|--|
| No. of samples              | 28   | 28   |
| Onset of plasma formation   | 3.7 J/cm <sup>2</sup>                              | 4.8 J/cm <sup>2</sup>                              |
| Radiant exposure range      | 1.5–3.6 J/cm <sup>2</sup>                          | 2.0–4.7 J/cm <sup>2</sup>                          |
| Correlation coefficient (r) | 0.975  | 0.996  |
| Slope                       | 267 $\mu\text{g/J}$<br>(242–292) <sup>a</sup>      | 300 $\mu\text{g/J}$<br>(290–311) <sup>a</sup>      |
| X-axis intercept            | 1.15 J/cm <sup>2</sup><br>(1.03–1.27) <sup>a</sup> | 1.47 J/cm <sup>2</sup><br>(1.41–1.54) <sup>a</sup> |

<sup>a</sup>95% Confidence interval.

mean thickness of thermal injury  $\pm 1$  standard deviation was  $34 \pm 9 \mu\text{m}$  and  $53 \pm 17 \mu\text{m}$  for TEA CO<sub>2</sub> irradiation at wavelengths 9.5  $\mu\text{m}$  and 10.6  $\mu\text{m}$ , respectively. The difference between these values was statistically significant (t-test,  $P = .002$ ).

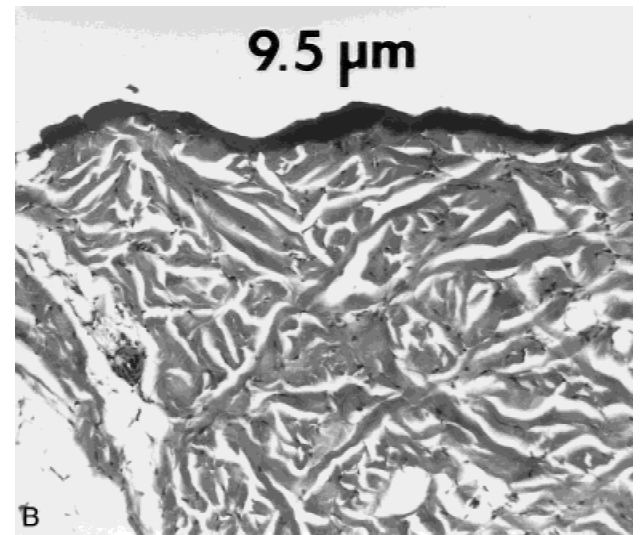
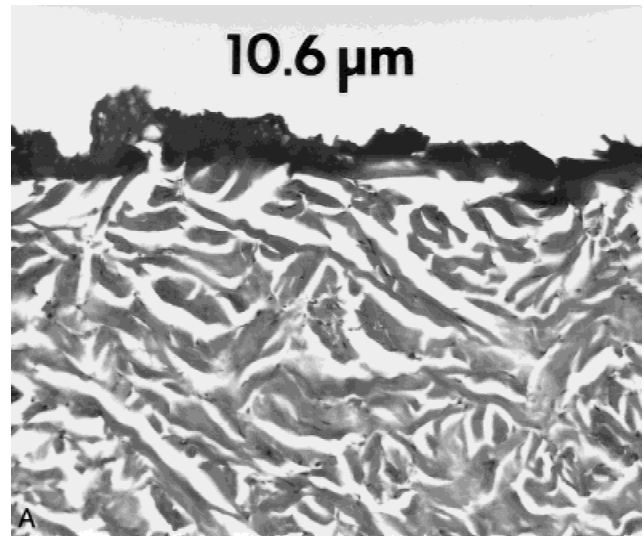


Fig. 5. Typical histology slides after 12 pulses of TEA CO<sub>2</sub> irradiation. The zone of thermal injury is approximately 60  $\mu\text{m}$  and 30  $\mu\text{m}$  for wavelengths 10.6  $\mu\text{m}$  (A) and 9.5  $\mu\text{m}$  (B), respectively.  $\times 100$ .

## DISCUSSION

This report describes tissue removal and thermal injury experiments performed on porcine dermis using TEA CO<sub>2</sub> laser irradiation at wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$ . At both wavelengths ablation appeared to be explosive, causing tissue fragments to collect on or near the ZnSe focusing lens. We had initially thought that by targeting collagen and tissue water equally using 9.5- $\mu\text{m}$  radiation, a surface vaporization event would occur, whereas an explosive event would occur when only tissue water was targeted using 10.6- $\mu\text{m}$  radiation. However, under our experimental conditions, it appears that sufficient laser energy was



available in the tissue water to produce explosive material removal at both wavelengths [8]. It follows that if collagen is more selectively targeted by using another wavelength, the energy absorbed by the tissue water will be small and may not be sufficient to cause explosive vaporization. Therefore, tissue chromophore, or more precisely, the ratio of absorption coefficients of the chromophores within the tissue volume, may govern ablation mechanism. This is presumably why ultraviolet irradiation is consistent with a process of rapid surface vaporization and not explosive vaporization [7]. However, the specific role of ablation mechanism on clinically relevant parameters such as ablation efficiency, threshold, and depth of thermal injury remains unclear.

The pulse duration used in this study was chosen to limit thermal diffusion out of the chromophore during irradiation, thereby allowing direct targeting or photothermolysis of the chromophore [19]. The time scale of thermal diffusion ( $\tau_d$ ) is given by  $\tau_d \approx \delta^2/\alpha$ , where  $\delta$  is the characteristic size of the chromophore and  $\alpha$  is the thermal diffusivity. Assuming the characteristic size of the chromophore (collagen fiber) is  $\approx 1 \mu\text{m}$ , and the thermal diffusivity is comparable to water, the time scale for thermal diffusion is  $\approx 7 \mu\text{s}$ . Therefore, to limit thermal diffusion during irradiation, the pulse duration must be less than  $7 \mu\text{s}$ . One should note that the pulse duration used in these experiments is considerably different from pulse durations used in many current dermatologic procedures.

The question still remains as to what determines the efficiency of an explosive ablation process. Explosive vaporization can be produced by a rapid phase transition to vapor from mechanically unstable superheated tissue water at the spinodal limit [8,20–23]. When phase separation occurs, very high pressures are generated which are comparable to the ultimate tensile strength (UTS) of porcine dermis (8–10 MPa) [24]. It follows that tissues with low tensile strength will be less likely to impede material removal, thereby allowing a more efficient ablation event. In other words, when phase separation occurs, the efficiency of material removal will directly depend on the tissue UTS. During 10.6- $\mu\text{m}$  irradiation, we speculate that the tissue structural matrix remains intact, and therefore produces a less efficient ablation process. However, during 9.5- $\mu\text{m}$  irradiation, the tissue structural matrix is compromised or weakened by directly targeting collagen, and consequently produces a more efficient ablation pro-

cess. These results are consistent with those of Walsh and co-workers who observed increased ablation efficiencies when irradiating tissues with lower ultimate tensile strength but equal optical absorption [25].

In our studies residual thermal injury appears to be inversely related to ablation efficiency. When compared to 10.6  $\mu\text{m}$ , 9.5- $\mu\text{m}$  irradiation resulted in a more efficient removal process with smaller residual thermal injury. This inverse relationship between ablation efficiency and depth of thermal injury is most easily explained by considering how the delivered laser energy is used. Laser energy must either contribute to the vaporization and ejection of ablated material or the heating of the remaining tissue, thereby producing thermal injury by denaturing tissue components. It follows that the more efficient the explosive ablation process the smaller the residual thermal injury. In other words, if a greater fraction of incident energy is used for tissue removal, a smaller fraction of incident energy is available to produce thermal injury. However, this inverse relationship may also depend on other factors such as absorption depth and tissue UTS.

Because the ablation mechanism appears to be consistent with explosive vaporization caused by metastable superheating for both wavelengths, ablation threshold should be governed only by the temperature of the tissue water. Therefore, the energy per unit volume within the tissue water at threshold should be the same for both 10.6  $\mu\text{m}$  and 9.5- $\mu\text{m}$  wavelengths (i.e., the threshold radiant exposure should scale with the absorption depth of water). The volumetric energy densities in the tissue water for wavelengths 10.6  $\mu\text{m}$  and 9.5  $\mu\text{m}$  are 690 J/cm<sup>3</sup> and 800 J/cm<sup>3</sup>, respectively, and are indeed comparable.

In summary, tissue removal was consistent with explosive vaporization for both 10.6- $\mu\text{m}$  and 9.5- $\mu\text{m}$  wavelengths. Although the ablation mechanism appeared to be the same, 9.5- $\mu\text{m}$  irradiation removed tissue more efficiently and with a smaller zone of thermal injury than at 10.6- $\mu\text{m}$  irradiation. These differences may be due to the weakening of the tissue mechanical strength by directly targeting collagen. Ablation threshold scaled directly with volumetric energy density or superheat temperature within the tissue water. The observation that one can reduce or enhance thermal injury with no change in ablation mechanism by simply tuning the CO<sub>2</sub> laser to a different laser line may have a significant impact for a variety of dermatologic applications.

## ACKNOWLEDGMENTS

The authors are grateful to Andrew Yablon for many helpful discussions and to Tom Flotte for his help with the histology analysis.

## REFERENCES

- Walsh JT, Jr, Flotte TJ, Anderson RR, Deutsch TF. Pulsed CO<sub>2</sub> laser tissue ablation: effect of tissue type and pulse duration on thermal damage. *Lasers Surg Med* 1988; 8:108–118.
- Fitzpatrick RE, Goldman MP, Satur NM, Tope WD. Pulsed carbon dioxide laser resurfacing of photoaged facial skin. *Arch Dermatol* 1996; 132:395–402.
- Waldorf HA, Kauvar ANB, Geronemus RG. Skin resurfacing of fine to deep rhytides using a char-free carbon dioxide laser in 47 patients. *Dermatol Surg* 1995; 21:940–946.
- Lowe NJ, Lask G, Griffin ME. Laser skin resurfacing. Pre- and posttreatment guidelines. *Dermatol Surg* 1995; 21:1017–1019.
- Puliafito CA, Wong K, Steinert RF. Quantitative and ultrastructural studies of excimer laser ablation of the cornea at 193 and 248 nanometers. *Lasers Surg Med* 1987; 7:155–159.
- Lane RJ, Wynne JJ, Torres A, Geronemus RG. Ultraviolet-laser ablation of skin. *Arch Dermatol* 1985; 121:609–617.
- Venugopalan V, Nishioka NS, Mikic BB. The thermodynamic response of soft biological tissue to pulsed ultraviolet laser irradiation. *Biophys J* 1995; 69:1259–1271.
- Venugopalan V, Nishioka NS, Mikic BB. Thermodynamic response of soft biological tissues to pulsed infrared-laser irradiation. *Biophys J* 1996; 70:2981–2993.
- Edwards G, Logan R, Copeland M, Reinisch L, Davidson J, Johnson B, Maciunas R, Mendenhall M, Ossoff R, Tribble J, Werkhaven J, O'Day D. Tissue ablation by a free-electron laser tuned to the amide II band. *Nature* 1994; 371:416–419.
- Srinivasan R, Dyer PE, Braren B. Far-ultraviolet laser ablation of the cornea: photoacoustic studies. *Lasers Surg Med* 1987; 6:514–519.
- Hahn DW, Ediger MN, Pettit GH. Dynamics of ablation plume particles generated during excimer laser corneal ablation. *Lasers Surg Med* 1995; 16:384–389.
- Srinivasan R. Ablation of polymers and biological tissue by ultraviolet lasers. *Science* 1986; 234:559–565.
- Ediger MN, Pettit GH, Weiblinger RP, Chen CH. Transmission of corneal collagen during ArF excimer laser ablation. *Lasers Surg Med* 1993; 13:204–210.
- Ediger MN, Pettit GH, Hahn DW. Enhanced ArF laser absorption in a collagen target under ablative conditions. *Lasers Surg Med* 1994; 15:107–111.
- Staveteig PT, Walsh JT, Jr. Dynamic 193-nm optical properties of water. *Appl Opt* 1996; 35:3392–3403.
- Yannas IV. Collagen and gelatin in a solid state. *J Macromol Sci Rev Macromol Chem* 1972; C7:49–104.
- Downing HD, Williams D. Optical constants of water in the infrared. *J Geophys Res* 1975; 80:1656–1661.
- Payne BP. The role of chromophore on pulsed laser ablation of biological tissue. In: "Mechanical Engineering." Cambridge: Massachusetts Institute of Technology: 1997, p 67.
- Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983; 220:524–527.
- Miotello A, Kelly R. Critical assessment of thermal models for laser sputtering at high fluences. *Appl Phys Lett* 1995; 67:3535–3537.
- Oraevsky AA, Esenaliev RO, Letokhov VS. Temporal characteristics and mechanism of atherosclerotic tissue ablation by nanosecond and picosecond pulses. *Lasers Life Sci* 1992; 5:75–93.
- Miotello A, Kelly R. Comments on explosive mechanisms of laser sputtering. *Appl Surf Sci* 1996; 96–98:205–215.
- Skripov VP. "Metastable Liquids." New York: John Wiley and Sons, 1974.
- Yamada H, "Strength of Biological Materials." New York: Robert E. Krieger, 1973.
- Walsh JT, Jr, Deutsch TF. Pulsed CO<sub>2</sub> laser ablation of tissue: effect of mechanical properties. *IEEE Trans Biomed Eng* 1989; 36:1195–1201.